UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,670	09/25/2007	Patrick W. Trown	006337.00021	4435

22907 7590 11/10/2009

BANNER & WITCOFF, LTD.
1100 13th STREET, N.W.
SUITE 1200
WASHINGTON, DC 20005-4051

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
11/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,670	TROWN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *14-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/9/06, 5/15/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response received September 4, 2009 is acknowledged.

Claims 1-56 are pending in the instant application.

Applicant's election of Group I, claims 1-13, 55, and 56, drawn to chimeric polypeptides in the reply filed on September 4, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 14-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 4, 2009 as explained above.

Claims 1-13, 55, and 56 are under examination in this office action.

Information Disclosure Statement

2. The IDS statements received 5/9/06 and 5/15/08 are acknowledged and have been considered.

Specification

3. The title is objected to as being too vague. A new title that better reflects the instant claimed invention is suggested. Specifically, the current title in no way suggests the instant claimed invention of fusion proteins comprising FVII and an IgG1 Fc domain.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the independent claim recites that the factor VII polypeptide comprises a mutation at specific positions. The frame of reference used for counting such that an artisan would know what residue is residue 152 is not specified. This would not be a problem if FVII polypeptides were defined as always being the same length as native full length FVII. However, paragraph 15 on page 5 states concerning the recited first and second polypeptides, "The polypeptides may comprise only so much of the full proteins as are necessary for functioning in the chimeric protein". The functions of the first and second are then defined as being binding to TF and mediating CDC responses respectively. Thus, the first FVII polypeptide conceivably could be smaller than 152 amino acids in length. As such, what position is mutated? The same can be said for the human IgG1 Fc domain, since Fc domains with complement activity can be made which are shorter than full length. Thus applicant should clearly state the frame of reference used for the numbering convention used in the claim. An example would be "...prevents...cleavage between residues...152 and 153 of full length human FVII". Many other reference frames can also be used to define the required mutated positions.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 55 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Garen (WO 01/02439, of record).

Garen discloses immunoconjugates which comprise mutated FVII as a targeting domain and the Fc domain of human IgG1 as an effector domain (see entire document, particularly the abstract, lines 1-15 of page 1, and example 2). The mutant FVII comprises active site mutations at K341, S344, or both, which reduce its blood coagulation activity while leaving binding to tissue factor unaffected (see particularly the abstract, page 4, page 11, and claim 1). It is disclosed that mutations to alanine at the active site residues are particularly favored (see particularly lines 11-25 of page 11 and claims 2 and 3). The immunoconjugates of Garen are further disclosed as being dimeric (see particularly Figure 1 and claim 1), and that the IgG1 domain provides for NK cell and complement mediated cytolytic activity against tissue factor expressing cells (see particularly the paragraph that spans pages 10 and 11 and examples 2 and 3).

Therefore, the prior art anticipates the claimed invention.

8. Claims 1, 2, 4, 6-8, 13, 55 and 56 are rejected under 35 U.S.C. 102(e) as being anticipated by Bjorn et al. (US 2004/0110929).

Bjorn et al. disclose immunoconjugates wherein human FVII is conjugated to human IgG1 (see entire document, particularly paragraphs 14, 23, 24, 29, examples 1-3, and claims 1-25). Forms of FVII disclosed for use in the immunoconjugates include forms comprising the R152E and S344A mutations which reduce the blood coagulation activity of FVII yet retain the ability to bind to tissue factor (see particularly paragraphs 35, 36, and 38). The immunoconjugates are further disclosed as being dimers (see paragraphs 36, 37, and 85). The immunoglobulin domains are disclosed as mediating

both complement and cell mediated lysis of target cells expressing tissue factor (see particularly paragraphs 66-78).

Therefore, the prior art anticipates the claimed invention.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-8 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garen (WO 01/02439, of record) in view of Wildgoose et al. (Biochemistry, 1990, 29:3413-20, of record).

The teachings of Garen have been discussed above and differ from the instant claimed invention in that Garen do not disclose FVII mutations at position 152.

Wildgoose et al. disclose that FVII molecules comprising the R152E mutation have markedly reduced ability to partake in the blood coagulation enzymatic cascade (see entire document, particularly the abstract).

Therefore, it would have been obvious to an ordinary artisan at the time the invention was made to incorporate the mutation disclosed by Wildgoose et al. into the constructs of Garen. This is because Garen discloses his constructs as comprising one or more mutations in FVII that reduce its ability to partake in the coagulation cascade,

and this same property is shared by the molecules of Wildgoose et al. Thus the ordinary artisan would know that more than one mutation inhibiting biological activity could be combined as per the teachings of Garen and would have a reasonable expectation of success in doing so since the mutations disclosed by Garen and the mutation of Wildgoose all share the same physiological activity of inhibiting FVII coagulation activity. Note that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also MPEP 2144.06.

It also would have been obvious to use additional mutations at the position disclosed by Wildgoose et al. in FVII. Specifically, an ordinary artisan would known that glutamate is structurally very similar to glutamine, and that neither is chemically similar to arginine in that neither Q or E are positively charged. Also, it is routine in the art to make mutants containing alanine, such as was done by Garen, since it comprises a small, non-polar side group (a single methyl group). Thus, it too is physically and chemically different from arginine in that it is much smaller and is not positively charged. Further, both Garen and Wildgoose et al. disclose exemplary methods by which mutants can be screened for activities. Thus, an ordinary artisan would reasonably expect R152Q and R152A mutants to share the biological properties of R152E mutants, namely that said mutants comprise inhibited ability to partake in thrombus formation.

11. Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garen (WO 01/02439, of record) in view of Idusogie et al. (US patent 6,528,624).

The teachings of Garen have been discussed above and differ from the instant claimed invention in that while Garen discloses that his immunoconjugates comprise cell mediated and complement mediated cytotoxicity, he does not disclose mutating positions within the Fc domain of the immunoconjugate to increase cytotoxic activity.

Idusogie et al. disclose that polypeptides, such as immunoconjugates, which comprise an Fc domain can be mutated at positions including 326 and 333 to increase cytotoxic effector function, such as complement mediated cytotoxicity mediated by C1q binding (see entire document, particularly the abstract and claims 12-15 and 18). Such mutations can occur singly or in combination, with the mutations of K326 to tryptophan and of E333 to serine being preferred (see particularly from line 27-58 of column 13 and claim 13).

Therefore, a person of ordinary skill in the art would be motivated to modify the immunoconjugates disclosed by Garen which have complement mediated cytotoxic activity to include the Fc mutations disclosed by Idusogie et al. since the Fc mutations increase cytotoxic activity and thus would be more effective when performing the therapeutic methods disclosed by Garen.

12. Claims 3, 5, and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bjorn et al. (US 2004/0110929) in view of Idusogie et al. (US patent 6,528,624).

The teachings of Bjorn et al. have been discussed above and differ from the instant claimed invention in that while Bjorn et al. disclose that their immunoconjugates comprise cell mediated and complement mediated cytotoxicity, they do not disclose mutating positions within the Fc domain of the immunoconjugate to increase cytotoxic activity. Bjorn et al. also do not disclose mutations a position 152 of FVII other than R152E.

Idusogie et al. disclose that polypeptides, such as immunoconjugates, which comprise an Fc domain can be mutated at positions including 326 and 333 to increase cytotoxic effector function, such as complement mediated cytotoxicity mediated by C1q binding (see entire document, particularly the abstract and claims 12-15 and 18). Such mutations can occur singly or in combination, with the mutations of K326 to tryptophan and of E333 to serine being preferred (see particularly from line 27-58 of column 13 and claim 13).

Therefore, a person of ordinary skill in the art would be motivated to modify the immunoconjugates disclosed by Bjorn et al which have complement mediated cytotoxic

activity to include the Fc mutations disclosed by Idusogie et al. since the Fc mutations increase cytotoxic activity and thus would be more effective when performing the therapeutic methods disclosed by Bjorn et al.

It also would have been obvious to use additional mutations at position 152 of FVII other than R152E. Specifically, an ordinary artisan would known that glutamate is structurally very similar to glutamine, and that neither is chemically similar to arginine in that neither Q or E are positively charged. Also, it is routine in the art to make mutants containing alanine since it comprises a small, non-polar side group (a single methyl group). Thus, it too is physically and chemically different from arginine in that it is much smaller and is not positively charged. Further, Bjorn et al. disclose exemplary methods by which mutants can be screened for activities. Thus, an ordinary artisan would reasonably expect R152Q and R152A mutants to share the biological properties of R152E mutants, namely that said mutants comprise inhibited ability to partake in thrombus formation.

13. No claims are allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is (571)272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Szperka, Ph.D.
Primary Examiner
Art Unit 1644

/Michael Szperka/
Primary Examiner, Art Unit 1644